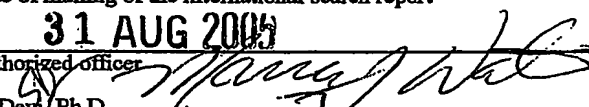


# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/37763

<b>A. CLASSIFICATION OF SUBJECT MATTER</b> IPC(7) : A61K 53/16, 35/14, 39/02, 38/00 US CL : 424/531, 530, 529, 831; 514/2, 921, 916 According to International Patent Classification (IPC) or to both national classification and IPC																										
<b>B. FIELDS SEARCHED</b> Minimum documentation searched (classification system followed by classification symbols) U.S. : 424/531, 530, 529, 831; 514/2, 921, 916  Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched  Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) Please See Continuation Sheet																										
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>																										
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.																								
X	WO 00/55350 A1 (HUMAN GENOME SCIENCES, INC.) 21 September 2000 (21.09.00), claims 17 and 11; pages 372-375, 395, 405 and 406; and abstract.	1-4 and 7-15																								
X,P	WO 2004/023973 A2 (INCYTE CORPORATION) 25 March 2004 (25.03.2004), entire document	1-4 and 7-15																								
<input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex.																										
<table border="0"> <tr> <td colspan="2">* Special categories of cited documents:</td> <td>"T"</td> <td>later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</td> </tr> <tr> <td>"A"</td> <td>document defining the general state of the art which is not considered to be of particular relevance</td> <td>"X"</td> <td>document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone</td> </tr> <tr> <td>"B"</td> <td>earlier application or patent published on or after the international filing date</td> <td>"Y"</td> <td>document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art</td> </tr> <tr> <td>"L"</td> <td>document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</td> <td>"&amp;"</td> <td>document member of the same patent family</td> </tr> <tr> <td>"O"</td> <td>document referring to an oral disclosure, use, exhibition or other means</td> <td></td> <td></td> </tr> <tr> <td>"P"</td> <td>document published prior to the international filing date but later than the priority date claimed</td> <td></td> <td></td> </tr> </table>			* Special categories of cited documents:		"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention	"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone	"B"	earlier application or patent published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art	"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family	"O"	document referring to an oral disclosure, use, exhibition or other means			"P"	document published prior to the international filing date but later than the priority date claimed		
* Special categories of cited documents:		"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention																							
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone																							
"B"	earlier application or patent published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art																							
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family																							
"O"	document referring to an oral disclosure, use, exhibition or other means																									
"P"	document published prior to the international filing date but later than the priority date claimed																									
Date of the actual completion of the international search 15 June 2005 (15.06.2005)		Date of mailing of the international search report <b>31 AUG 2005</b>																								
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230		Authorized officer  S. Dev, Ph.D. Telephone No. (703) 308-0196																								

**INTERNATIONAL SEARCH REPORT**

International application No.  
PCT/US04/37763

Continuation of B. FIELDS SEARCHED Item 3:

WEST, DIALOG, MEDLINE, BIOSIS, EMBASE, Sequence databases

Gelsoxin, SEQ ID NO: 1 and fragments thereof, (LPS or lipopolysaccharide), sepsis, shock, Gram negative bacterial infect?, inventors' names

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/37763

### Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:  
Claims 16 and 26 are improperly multiple dependent.
3. ☒ Claims Nos.: 16 and 26  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

### Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:  
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-4 and 7-15

Remark on Protest

☐  
☐

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/37763

### BOX III. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claims 1-4 and 7-15, drawn to a method of increasing the concentration of gelsolin or functionally equivalent peptide fragment thereof, or reducing endotoxemia in a patient by administering gelsolin or functionally equivalent peptide fragment thereof.

Group II, claims 1, 5, 7 and 8, drawn to a method of reducing the inhibition of fibrinolysis comprising administering a gelsolin-containing actin-binding compound.

Group III, claims 1 and 6-8, drawn to a method of restoring or maintaining normal aggregation of platelets in a patient by administering gelsolin or functionally equivalent peptide fragment thereof.

Group IV, claims 17-21, drawn to a method of preventing pathogenesis of microvascular dysfunction, ARDS or venous obstruction by administering gelsolin or functionally equivalent peptide fragment thereof.

Group V, claims 22 and 23, drawn to a method of predicting adverse clinical outcome associated with massive inflammation in a patient by measuring the circulating gelsolin concentration.

Group VI, claims 24 and 25, drawn to a pharmaceutical composition comprising gelsolin or a functionally equivalent peptide fragment thereof and a pharmaceutically acceptable vehicle.

Claims 16 and 26 are unsearchable because of their improper multiple dependency.

The inventions listed as Groups I-VI do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Claims 16 and 26 are unsearchable because of their improper multiple dependency.

Inventions I-VI lack unity. The special technical feature of the first claimed invention is a method of increasing the concentration of gelsolin or functionally equivalent peptide fragment thereof, or reducing endotoxemia in a patient by administering gelsolin or functionally equivalent peptide fragment thereof. However, such a method involving administration of gelsolin or functionally equivalent peptide fragment thereof was already disclosed in the art at the time of the invention. For example, WO 00/55350 A1 (HUMAN GENOME SCIENCES, INC.) disclosed a method of preventing, treating, or ameliorating a medical condition, such as, Gram negative bacterial infections, infection-induced sepsis and septic shock comprising administering to a mammalian subject of a therapeutically effective amount of a polypeptide comprising the instantly recited SEQ ID NO: 1, AAB43620 (see claims 11 and 17; pages 372-375, 395, 405 and 406; and abstract). Such a method would be expected to reduce the concentration of Gram negative bacterial LPS in the patient. Thus, the special technical feature of the first claimed method is taught by the prior art, and therefore does not define over the prior art. The special technical features of subsequently claimed inventions are delineated above. The methods of inventions II-V do not share significant common steps and ultimate goals accomplished. The special technical feature of invention VI is a pharmaceutical composition comprising gelsolin or a functionally equivalent peptide fragment thereof and a pharmaceutically acceptable vehicle, which is also disclosed by WO 00/55350 A1 (HUMAN GENOME SCIENCES, INC.).